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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,015	04/18/2006	Claudio Soto-Jara	ARS-102	4494

23557 7590 10/17/2007

SALIWANCHIK LLOYD & SALIWANCHIK
A PROFESSIONAL ASSOCIATION
PO BOX 142950
GAINESVILLE, FL 32614-2950

EXAMINER	
STOICA, ELLY GERALD	
ART UNIT	**PAPER NUMBER**
1647	

MAIL DATE	DELIVERY MODE
10/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,015	SOTO-JARA ET AL.	
	Examiner	Art Unit	
	Elly-Gerald Stoica	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-39,47,51 and 56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-39 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I (claims 35-39 and 46) and of the species SEQ ID NO: 6 or a peptide sequence comprising between 5 and 10 amino acids, or an active mutant thereof, a fusion polypeptide or peptide thereof, or derivative thereof, in the reply filed on 08/23/2007 is acknowledged. The traversal is on the grounds that the common or corresponding special technical feature for this invention is the ability of the peptides presented in claim 35 to bind to the OX40R and have the ability to interfere with the binding of OX40L with OX40R. This is not found persuasive because, as previously iterated, the OX40L sequence was known as ACT-4-L in the art (WO/95/21915) and the full length of the protein may be construed as a precursor, as in claim 1, h of the originally presented claims.

The requirement is still deemed proper and is therefore made FINAL.

Status of the claims

2. Claims 40-46, 48-50 and 52-55 were cancelled. Claims 35-39, 47, 51, and 56 are pending. Claims 51 and 56 are withdrawn. Claims 35-39 and 47 are subject to examination.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 35-39 and 47are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Specifically, the claims encompass an isolated polypeptide consisting of:

a) amino acids 94-124 of human OX40 ligand (OX40L) ;

b) a peptide sequence of human OX40L of between 5 and 10 amino acids that binds to OX40R;

c) an active mutant of a) or b) wherein one or more of the amino acids has been conservatively substituted and said active mutant binds to OX40R;

Also claimed is an isolated peptide designed on the sequence, the structure or the sequence and structure of an amino acid sequence corresponding to 107-116 (SEQ NO ID: 8) or 107-111 (SEQ ID NO: 13) of human OX40L.

Thus, the claims are drawn to a genus of peptides that are defined by their functionality. The sequence defined by Sequence Id. Nos.: 6, 8 and 13 also provide structural limitations. The above sequences claimed (i.e., a peptide sequence between 5 and 10 amino acids that binds to OX40R, an active mutant or fusion proteins or derivatives containing them) do not have adequate written description.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics

of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is the functionality of the claimed peptides. With the exception of the peptides having Seq. Id. Nos.: 6, 8 and 13 there is no identification of any particular portion of the structure that must be conserved and linked to the functionality of the peptide. There is no requirement for the peptides of 5 to 10 amino acids with regard to the structure or the region of the protein that they are part of apart for the description of the Seq. Id. Nos.: 6, 8 and 13. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

Therefore, only the peptides having the Seq. Id. Nos.: 6, 8 and 13 but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description

provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 35-39 and 47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Since the claims lack adequate written description for peptides other than the ones having Seq. Id. Nos.: 6, 8 and 13, the meets and bounds of the claims could not be established. Specifically, for part c) of the claim 35, the written description of a sequence of 5 to 10 amino acids without properly addressing structure function limitation (apart from the Seq. Id. Nos.: 8 and 13) is inadequate. It is unclear if the 5-10 amino acids have to have contiguity, if they have a conserved portion to be present or if any random 5 or 10 oligomer that binds to OX40L would meet the limitations of the claim. Thus peptides defined just by 5 to 10 amino acid from anywhere in the OX40L could not be adequately searched.

In part a) of claim 35, the parenthetical (Seq. Id. No.: 6) would not let one to clearly determine if it refers to the sequence of OX40L, to the positions 94-124 from the amino acid sequence of the human OX40L, or to the positions 94-124 of any sequence that is aligned with the sequence of the OX40L. In part b) of the claim 35, it is unclear if the one or more amino acids contiguous that are to be deleted are contiguous or not. For part e) of claim 35, it is unclear if the recitation "one or more" may include the

situation in which all the amino acids may be substituted. For part g), it is unclear what the metes and bounds of "a derivative" are.

In claim 38, it is unclear how a polypeptide may comprise a solid support.

For claim 39, the recitation "designed on the sequence" is unclear. It does not inform the reader of the metes and bounds of what is being claimed, as "designed" is a mental step, without any indicator of a process or result. The manner of obtaining a compound does not, in this case, describe the compound so obtained.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 35-39 and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Godfrey et al. (U.S. Pat. 6,242,566).

Godfrey et al. teach purified ACT-4-L (which is an earlier name for OX40L- as acknowledged by Applicant) ligand polypeptides; an exemplified ACT-4-L ligand designated ACT-4-L-h-1. The polypeptide of Seq. Id. No.: 6 of the instant Application is 100% identical with the amino acid string 94-124 of the Seq. Id. No.: 4 of Godfrey et al.

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 RESULT 5
US-08-195-967-4
; Sequence 4, Application US/08195967
; Patent No. 6242566
;  GENERAL INFORMATION:
;    APPLICANT:  Godfrey, Wayne
;    APPLICANT:  Engleman, Edgar G.
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;     TITLE OF INVENTION:  LIGAND (ACT-4-L) TO A RECEPTOR ON THE SURFACE OF
ACTIVATED
;     TITLE OF INVENTION:  CD4+ T-CELLS
;     NUMBER OF SEQUENCES:  4
;     CORRESPONDENCE ADDRESS:
;       ADDRESSEE:  Townsend and Townsend Khourie and Crew
;       STREET:  379 Lytton Avenue
;       CITY:  Palo Alto
;       STATE:  California
;       COUNTRY:  US
;       ZIP:  94301
;     COMPUTER READABLE FORM:
;       MEDIUM TYPE:  Floppy disk
;       COMPUTER:  IBM PC compatible
;       OPERATING SYSTEM:  PC-DOS/MS-DOS
;       SOFTWARE:  PatentIn Release #1.0, Version #1.25
;     CURRENT APPLICATION DATA:
;       APPLICATION NUMBER:  US/08/195,967
;       FILING DATE:  10-FEB-1994
;       CLASSIFICATION:  424
;     ATTORNEY/AGENT INFORMATION:
;       NAME:  Smith, William M
;       REGISTRATION NUMBER:  30,223
;       REFERENCE/DOCKET NUMBER:  05490A-230
;     TELECOMMUNICATION INFORMATION:
;       TELEPHONE:  (415) 326-2400
;       TELEFAX:  (415) 326-2422
;   INFORMATION FOR SEQ ID NO:  4:
;     SEQUENCE CHARACTERISTICS:
;       LENGTH:  183 amino acids
;       TYPE:  amino acid
;       TOPOLOGY:  linear
;     MOLECULE TYPE:  protein
US-08-195-967-4

  Query Match             100.0%;  Score 165;  DB 2;  Length 183;
  Best Local Similarity   100.0%;  Pred. No. 4.7e-17;
  Matches   31;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps
0;

Qy          1 IINCDGFYLISLKGYFSQEVNISLHYQKDEE 31
              |||||||||||||||||||||||||||||||
Db         94 IINCDGFYLISLKGYFSQEVNISLHYQKDEE 124
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Godfrey et al. also teach purified extracellular domains of ACT-4-L ligands. These domains comprise at least five contiguous amino acids from the full-length ACT-4-L-h-1 extracellular domain. Some extracellular domains consist essentially of a

domain possessing a particular functional property, for example, the capacity to specifically bind to the ACT-4-h-1 receptor expressed on the surface of $CD4^+$ T-cells. Any of the above extracellular domains may further comprise a linked second polypeptide such as the constant region of an immunoglobulin heavy chain (col. 2, line 46 to col. 3, line 5). Also described by Godfrey et al. are ligands representing allelic, nonallelic, splice and higher cognate variants of ACT-4-L-h-1, and natural or induced mutants of any of these. Such variants will typically show substantial sequence identity with the ACT-4-L-h-1 sequence, and contain at least 4 and more commonly 5, 6, 7, 10 or 20, 50 or more contiguous amino acids from the ACT-4-L-h-1 sequence (col. 12, lines 15-22). Besides the full-length polypeptides, Godfrey et al. teach biologically active fragments of full-length ACT-4-L ligand polypeptides (synonymous to active mutant of the instant application). Significant biological activities include binding to an ACT-4 receptor such as ACT-4-h-1 and a segment of a full-length ACT-4-L ligand polypeptide will ordinarily comprise at least 5 contiguous amino acids of the ACT-4-L (col.13, lines 21-38). Godfrey et al. also disclose fusion partners for the ACT-4-L polypeptides that include toxins (e.g., diphtheria toxin, Pseudonomas ectotoxin A, ricin toxin or phospholipase C) and immunoglobulin components. The recombinant globulins formed by fusion of ACT-4-L fragments and immunoglobulin components often have most or all of the physiological properties associated with the constant region of the particular immunoglobulin class used (col. 14, lines 58-59, col. 10, lines 43-53). The fusion proteins can be used to immobilize the peptide by the way of recombinant globulins, for binding analysis (i.e., solid support) (col. 11, lines 1-3; col.14, lines 64-67;col. 23, lines

1-3). Godfrey et al. also teach pharmaceutical compositions containing fragment s of the ACT-4-L and suitable pharmaceutical excipients, carrier, stabilizers, etc (col. 24, line 63 to col. 24 line13).

Therefore, Godfrey et al. anticipates the claims 35-39 and 47 of the instant Application.

9. Claims 35-36 are rejected under 35 U.S.C. 102(b) as being anticipated by O'Hare et al. (U.S. Pat. No.: 6,017,735).

O'Hare et al. teach coupled fusion proteins for intracellular transport, that include an amino acid sequence with the transport function of herpesviral VP22 protein and an immunomodulating protein sequence (abstract). The immunomodulatory protein to be coupled with VP22 can be itself a hybrid or fusion protein that can be, comprise, or correspond in functionality to the gp34 protein identified as a binding partner to human Ox40. The version of the gp34 protein functionality is a natural gp34 sequence itself, or to a fragment thereof, or to a hybrid expression product e.g. based on the (C terminal) extracellular (binding) domain of gp34 fused to another protein, e.g. to the constant region of an immunoglobulin heavy chain such as human IgG1, e g. with the extracellular domain of gp34 (a type 2 membrane protein) fused at its N-terminal to the C-terminal of the immunoglobulin constant domain (col. 13, lines 10-29).

GP 34 is a synonym for OX40L- as acknowledged by Applicant. Therefore, O'Hare et al. anticipates the claims 35-36 of the instant Application.

10. Claims 35 and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Godfrey et al. (J. Exp. Med. 180, 757-762, 1994).

Godfrey et al. disclose the human OX-40 ligand, which comprises in its sequence the Seq. Id. No.: 6 of the instant Application. On page 760, fig. 2, Godfrey et al. described the sequence 51-183 of the OX40L as being the extracellular region of the protein and, by inference, the portion of the polypeptide implicated in the binding to the OX 40- its receptor.

11. Claims 35, 36 and 47 rejected under 35 U.S.C. 102(b) as being anticipated by Weinberg et al. (U.S. Pat. 6, 312, 700).

Weinberg et al. teach a fusion between OX-40L extracellular domain and a polypeptide representing a constant domain of human IgG, particularly the CH2 and CH3 domains of IgG (col. 9, lines 24-44). Also taught are pharmaceutical compositions containing the OX-40 receptor binding agent (i.e., OX40L), combined with a pharmaceutical excipient, carrier or diluent (col. 13, lines 16-19).

Therefore, claims 35, 36 and 47 are anticipated by Weinberg et al.

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Chien et al. (Proc. Natl. Acad. Sci. USA, 88, 9578-9582, 1991), and Weinberg et al. (U.S. Pat. 6, 312, 700). Chien et al. teach the two-hybrid system- a method to identify proteins or protein fragments that interact with a protein of interest. Weinberg et al. teach a fusion between OX-40L extracellular domain and a polypeptide representing a constant domain of human IgG, particularly the CH2 and CH3 domains

of IgG (col. 9, lines 24-44). Also taught are pharmaceutical compositions containing the OX-40 receptor binding agent, combined with a pharmaceutical excipient, carrier or diluent (col. 13, lines 16-19).

Conclusion

13. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elly-Gerald Stoica whose telephone number is (571) 272-9941. The examiner can normally be reached on 8:30-17:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER